REMARKS

Review and reconsideration on the merits are requested.

Applicants appreciate the Examiner returning partially initialed SB/08 forms.

Applicants note the Examiner did not initial the Akayama et al and Takeda et al references listed in the SB/08 filed September 22, 2006. Clarification is requested.

Status of Claims

Claims 1-18 were pending at the time of the Action.

Claims 1-10, 15, 16 were 18 are withdrawn from consideration.

Claims 11-14 and 17 were rejected.

Claim 19 is newly added.

DETAILED ACTION

Claim Rejections - 35 U.S.C. § 112

First Paragraph

In greatly summarized form, the following aspects of the invention are not found to be enabled by the Examiner:

Preventing urinary incontinence;

Administering a *hydrate or solvate*.

Applicants simply delete the term "prevention or" and ", or a hydrate or a solvate thereof" in claim 11.

Withdrawal is requested.

Claim Rejections - 35 U.S.C. § 112

Second Paragraph

The Examiner finds "characterized by" in claim 11 to be indefinite and suggests replacing it with --comprising-- which would obviate the issue.

Claim 11 is so amended.

Withdrawal is requested.

The Prior Art

WO 00/02846 Tanaka et al, cited as a functional equivalent is U.S. 6,538,152 Tanaka et al (Tanaka) and Drug Discovery World, Fall 2003 (Ford) and U.S. 6,410,554 Broten et al (Broten); Mesh Supplementary Data (2009), referred to as Mesh.

Applicants discuss the obviousness rejections in the order posed.

The rejections are respectfully traversed.

The Examiner's position is set forth in the Action and will not be repeated here except as necessary to an understanding of Applicants' position which is now presented.

Rejection of Claims 11-14 and 17 Under 35 U.S.C. § 103(a) over Tanaka and Ford

Traversal

Applicants assume *arguendo* that Tanaka contains the teaching that the Examiner urges.

The Examiner states that Ford teaches the use of silodosin for the treatment of urinary incontinence based on Table 2B in Ford. Applicants consider, however, that Table 2B in fact only discloses that silodosin, an α_{1A}-adrenoceptor antagonist, is in Phase III clinical development for BPH/LUTS, but does not disclose anything about urinary incontinence.

Further, Table 2B simply lists drugs in development and does not give any specific disclosure on what kind of effect silodosin would exert on BPH/LUTS. Therefore, one of ordinary skill in the art would not know if silodosin was useful for urinary frequency or incontinence from any teaching in Ford at the time.

Further, Ford states:

"In a similar vein, selective α1-adrenoceptor antagonists are being explored for BPH/LUTS. Of the three subtypes - A, B and D - the A sybtype is prominent in urinary-outlet tissues. Despite this, the efficacy of α1-adrenoceptor antagonists has been disappointing, according to a number of companies and as published by Roche[9]." (see page 14, right column, the last paragraph).

A copy of Reference 9 from Ford (Blue, D, ..Ford, A, et al., J. Urol. 2002; 167(4); 265) is attached. In Reference 9, Ford et al concluded:

"Nevertheless, RO failed to produce any clinically significant symptomatic improvement thereby suggesting α_{A1}-AR antagonists will have little or no clinical utility in the treatment of BPH" (see Conclusions - the last two lines of Conclusions at the bottom of the page).

This not only shows that Table 2B does not suggest the efficacy of silodosin for BPH/LUTS, but in fact teaches away from such efficacy.

Withdrawal is requested.

Rejection of Claims 11-14 and 17 Under 35 U.S.C. § 103(a) as Being Unpatentable Over Tanaka in view of Broten in Light of Mesh

Traversal

Tanaka and Broten

Applicants have earlier commented on Tanaka and turn immediately to Broten.

Broten discloses that the use of a selective alpha-la adrenergic receptor antagonist in combination with a subtype non-selective endothelin antagonist provides relief of lower urinary tract symptoms (LUTS) in patients with symptomatic prostatism or BPH.

Broten further discusses that such combination therapy improves LUTS, including increasing urine flow rate, decreasing residual urine volume and improving overall obstructive and irritative symptoms in patients with BPH or symptomatic prostatism (see from col. 6, line 4 from the bottom of the page to col. 7, line 2). One of ordinary skill in the art would clearly understand from the term "this combination therapy improves" that Broten at best teaches the effects as being expected from the combined use with an endothelin antagonist, not from an alpha-1a antagonist.

As effects expected from an alpha-la antagonist, Broten describes that an alpha-la adrenergic receptor antagonist is useful in treating BPH, inhibiting contraction of the lower urinary tract tissue (see col. 7, lines 36-41), and inhibiting the intrauretheral pressure response to phenylephrine (an alpha adrenergic agonist) (see Example 14).

However, since all these effects are related to inhibiting the contraction of the lower urinary tract, one of ordinary skill in the art might expect an effect of **relaxing the urinary tract and improving urine outlet** such as increasing urine flow rate and improving obstructive symptoms, but one of ordinary skill in the art would not expect any effect regarding treating urinary frequency or incontinence.

As a consequence, Applicants respectfully submit that one of ordinary skill in the art would not find it obvious to predict that silodosin would be useful for urinary frequency or incontinence from any teaching in Broten.

Applicants accept the Examiner's characterization of Mesh.

Withdrawal is requested.

Unexpected Results Established by Data in the Specification

Unexpected results are established by data in the specification.

Specifically, as shown in Example 2 and Figure 2, the changes in the micturition interval were 163.8%, 99.5%, 115.2% and 116.3% in the combination group of silodosin and compound 2, control group, silodosin administration group and compound 2 administration group, respectively.

From these results, one can calculate the differences in the change in micturition interval between control group and each of other groups, which are shown in the following table.

(%)	Control group	Silodosin group	Compound 2 group	Combination group
Change in micturition interval	99.5	115.2	116.3	163.8
Difference from control group	-	+15.7	+16.8	+64.3

As one of ordinary skill in the art would clearly understand from the above table, a synergistic improvement in the micturition interval was demonstrated by combination group in comparison with monotherapy by silodosin or compound 2. Such a superior effect would not be expected by one of ordinary skill in the art in any fashion.

Considering all of the above, withdrawal is requested.

Conclusion

From the earlier discussion, Applicants are of the strong view that there is no reasonable motivation for one of ordinary skill in the art to use silodosin for treating urinary frequency or incontinence, nor would one of ordinary skill in the art find obvious a method for the treatment of urinary frequency or incontinence which comprises administering silodosin in combination with a phenoxyacetic acid derivative (I) of the present invention, and this would be the case from the combination of Tanaka with Ford or Tanaka with Broten.

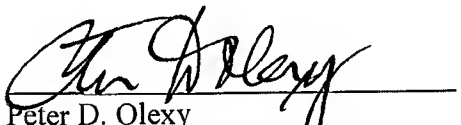
Further, since the presently claimed invention exhibits unexpectedly superior results as established above, it is submitted to be unobvious over the combination of references relied upon by the Examiner.

Withdrawal is requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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